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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/740,694	12/22/2003	Murty N. Arimilli	18477.031 / 259.PC2	1095

28381 7590 09/11/2007

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
09/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/740,694	ARIMILLI ET AL.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,30-33,62-65,93-96 and 123-125* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 96* is/are rejected.

7)☒ Claim(s) *30-33,62-65,93-95 and 123-125* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/27/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the amendment filed 22 June 2007. Claims 3, 30-33, 62-65, 93-96, and 123-125 are pending and examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 1, 2, 30-33, 62-65, 93-95 and 123-125 under 35 U.S.C. §112, second paragraph, as being indefinite is **withdrawn** in response to the Applicants' amendment.

The rejection of claim 1 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement is **withdrawn** in response to the claim cancellation.

The rejection of claim 1 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification commensurate in scope is **withdrawn** in response to the claim cancellation.

NEW REJECTION: Claims 3 and 96 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claims

contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*, (4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention*. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." M.P.E.P. §2163.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 199 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly & Co.,* the court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus.

Although the M.P.E.P. does not define what constitutes a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are directed to a method for identifying a candidate compound as a suitable pro-drug using an extract of peripheral blood mononuclear cells (PBMC) having carboxylic ester hydrolase activity to convert a candidate compound into a metabolite compound. The claims are drawn to genus of carboxylic ester hydrolases that are only defined by the process of extraction from PBMC, which contain a few different ester hydrolases.

The only factor present in the specification is the physical and/or chemical properties, a molecular weight around 70-100 kDa, and a pI around pH 4.5-5.5 (p.1694-1698) of GS-7340 ester hydrolase. The specification provides description for a single method of isolation, which yields an extract comprising ester hydrolysis activity when tested with the candidate compound GS-7340.

The genus of carboxylic ester hydrolases contains about 79 different enzymes. The single method of isolation of PBMC extract does not reflect the variance in this genus because the specification does not identify the characterized vs. the uncharacterized and the known vs. the unknown carboxylic ester hydrolases in the claimed PBMC extract. Accordingly, it is deemed that the specification fails to provide adequate written description for the entire genus of the carboxylic ester hydrolase from

PBMC and does not reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the entire genus in the claimed invention.

This rejection can be obviated by amending the claims to recite "a partially purified fraction of a PBMC extract comprising GS-7340 Ester Hydrolase activity."

NEW REJECTION: Claims 3 and 96 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a method comprising contacting a candidate compound with a partially purified fraction of a PBMC extract comprising GS-7340 Ester Hydrolase, does not reasonably provide enablement for an assay using any other PBMC extracted ester hydrolase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP §2164.01(a)). In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential

that every factor be examined in detail, those factors deemed most relevant should be considered.

The nature of the invention is a method for identifying a candidate compound as a suitable pro-drug comprising contacting a candidate compound having an esterified phosphonate group or an esterified carboxyl group, with an extract capable of catalyzing the hydrolysis of a carboxylic ester to produce a metabolite compound. The breadth of claims encompasses all carboxylic ester hydrolase activities in peripheral blood mononuclear cells (PBMC), including the unknown and uncharacterized carboxylic ester hydrolases from PBMC.

The description in the instant application does not support the entire scope of claimed invention. The specification only discloses one working example (page 1689-1698) involving contacting compound GS-7340 with a specific PBMC enzyme designated as GS-7340 Ester Hydrolase, along with the protocols for PBMC extraction and chromatography purification. This working example does not support the full breadth of the claims especially since there is one purification step that removes nonspecific ester hydrolases capable of cleaving alpha-naphthyl acetate. There is no direction or guidance on how to isolate or purify and use any other types of carboxylic ester hydrolase from PBMC extract to catalyze the hydrolysis of an esterified carboxylic or phosphonate group in the claimed candidate compound and produce the metabolite compound. Therefore, the amount of guidance does not correlate with the enzyme genus in claims 3 and 96.

The state of prior art is limited to carboxylic ester hydrolase activity in human monocytes (Lam *et al.*, 1978) and is silent on whether such hydrolase activity is specific for the claimed candidate compound having an esterified phosphonate group or an esterified carboxyl group.

Given the limited guidance in the specification and teaching in the art, one skilled in the art would be burdened with undue and unpredictable experimentation to identify all carboxylic ester hydrolases in PBMC extracts by trial and error. Absent working examples and specific teachings in the art regarding all PBMC ester hydrolases, those in the art would not be able to use the claimed method.

This rejection can be obviated by amending the claims to recite "a partially purified fraction of a PBMC extract comprising GS-7340 Ester Hydrolase activity."

Allowable Subject Matter

Claims 30-33, 62-65, 93-95 and 123-125 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
31 August 2007

Louise Humphrey, Ph.D.
Assistant Examiner